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TITLE: Prostate Cancer Biorepository Network

PRINCIPAL INVESTIGATOR: Jonathan Melamed, MD

RECIPIENT: New York University
New York, NY 10016

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PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

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6. AUTHOR(S)
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5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

New York University School of
Medicine
550 First Avenue
New York, NY 10016

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

The goal of this proposal is to contribute as a network site to the continued development of infrastructure and operations of the Prostate Cancer Biorepository Network (PCBN). The aim of the PCBN is to provide prostate researchers with high-quality, well-annotated biospecimens obtained in a systematic, reproducible fashion using optimized and standardized protocols. The PCBN is funded as a consortium of participating network sites that includes New York University, under the overall guidance of the coordinating center at Johns Hopkins. The NYU network site works collaboratively to contribute to the PCBN goals, through infrastructure development, biospecimen accrual and biospecimen specialized processing and disbursement to investigators. The NYU network site procures specimens from more than 3 facilities, from primary localized as well as metastatic prostate cancer patients and stores them to maintain high quality biospecimens. Additionally, clinical data including pathology and outcome data are annotated with the biospecimens. Specialized processing consists of tissue microarray design and construction. Biospecimens (mainly tissue microarrays) are disbursed to investigators approved through the PCBN. The combined efforts of the network site enables the PCBN consortium to successfully provide much sought after biospecimens for prostate cancer research.

15. SUBJECT TERMS

Prostate Cancer, Biorepository, tissue microarrays, tissue bank

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE		19	19b. TELEPHONE NUMBER *(include area code)*

Standard Form 298 (Rev. 8-98)
Prescribed by ANSI Std. Z39.18

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1. INTRODUCTION:

The goal of this proposal is to contribute to the continued development of infrastructure and operations of the Prostate Cancer Biorepository Network (PCBN). A prostate cancer biorepository fulfils an important need to enable prostate cancer research to be conducted by the wider research community due to the unavailability of biospecimens. Only few academic centers with high volume prostate cancer clinical services and an already developed banking infrastructure are well positioned to enable biospecimen collection. An external funding source as provided by the DOD enables support for a consortium of institutional biorepositories that can provide to the wider research community.

The major goal of the PCBN is to develop a biorepository with high-quality, well-annotated biospecimens obtained in a systematic, reproducible fashion using optimized and standardized protocols. The PCBN is funded as a consortium of participating network sites that include: New York University, Johns Hopkins, University of Washington and Memorial Sloan Kettering, under the overall guidance of the coordinating center at Johns Hopkins. The goal of the NYU network site is to collaboratively contribute toward the PCBN goals, through participation in infrastructure development, biospecimen accrual and derivative product development for the purpose of disbursement to investigators to enhance prostate cancer research. The efforts toward these goals are detailed herein.

2. KEYWORDS: Provide a brief list of keywords (limit to 20 words).

Prostate cancer, biorepository, biomarkers, tissue microarrays, tissue bank, rapid autopsy, advanced cancer, ethnicity

3. ACCOMPLISHMENTS: The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction.

Task 1. *Review of sources of patients and biospecimens at site that can be made available to the repository (Month 1): Completed in 1st quarter (October 2014)*

Task 2. *Data elements used to annotate demographic, clinical, pathology, and biospecimen life cycle will be provided to the Coordinating Center, and the Network Site will participate in in the process of defining and harmonizing a set of common data elements (CDEs): Completed in 1st quarter (October 2014)*

Task 3. *Submit SOPs currently in use to Coordinating Center (Month 1): Completed in 1st quarter (October 2014)*

Task 4. *Participate in development of draft SOPs, common consent formats, and MTA (Months 1-6): Completed in 1st quarter*

Task 5. Report on performance metrics (Month 6): Ongoing (accrual reports provided on quarterly basis)

Task 6. Continue offering existing biospecimens to the research community (Months 6-36): Ongoing – we continue to offer biospecimens to the research community.

Task 7. Participate in SOP training (Month 9): New staff trained in SOPs in first and second quarter (100%)

Task 8. Annotate, perform quality control for processing, storage and clinical data collection, and distribute specimens (Months 10-36): Quality control steps for data collection performed (20%)

Task 9. Report on performance metrics (Months 12, 18, 24, 30, 36): Month 24 reported herein (month 12 and prior quarterly reports previously submitted)

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Major activities:
The major activities of the NYU network site are detailed under the following areas
A) Regulatory approval
B) Biospecimen accrual
C) Specimen characterization and data annotation
D) Specialized processing of biospecimens
E) Biospecimen disbursement

A. Regulatory Approval:

NYU Medical Center

Regulatory approval: The NYU site includes several hospital facilities, each of which requires its own approval for conduct of activities. NYU has access to three hospitals: NYU Langone Medical Center, Bellevue (an HHC hospital) and the New York Harbor VA hospital and active case recruitment is performed at all sites; each with its own regulatory oversight.

The NYU PCBN maintains compliance with IRB issues at NYU Langone Medical center and Bellevue Hospital in accordance with the NYU IRB. Details of these activities over the last year are summarized below (table 1)

Table 1a: Regulatory Approval NYU/BH 10/1/2015- 9/30/16	Date Submitted	Date Approved
NYU IRB Annual Review	2/2/16	2/8/16
Bellevue Hospital IRB Annual Review	5/31/16	7/1/16
HRPO (A-18319.a)	2/22/16	3/3/16
Modification 42 – addition of personnel (Diane Wisniewski)	2/8/16	2/10/16
Modification 43 – waiver of authorization to monitor appt. schedules	3/25/16	4/15/16
Modification 44 – addition of personnel (Raveena Vakil)	6/23/16	6/24/16
Modification 45 – removal of personnel (Lina Kleyn)	8/9/16	8/10/16
Modification 46 –Translation of consents into Chinese (Mandarin)	8/25/16	8/31/16
Modification 47 – Approval for distribution of Patient Newsletter	9/9/16	9/15/16
Modification 48 –Translation of consents into Spanish	9/22/16	9/30/16

NY VA

The NYU PCBN maintains compliance with IRB issues at the Manhattan and Brooklyn VA Hospitals in accordance with the New York Harbor VA IRB. Details of these activities over the last year are summarized below (table 1b)

Table 1b:Regulatory Approval at VA over last year	Date Submitted	Date Approved
VA IRB Annual Review	6/30/16	8/22/16
VA Subcommittee for Human Studies Annual Review	6/24/16	7/5/16
HRPO (A-18319.b)	8/26/16	9/2/16
Clarification on protocol for consent for candidates for rapid autopsy	2/1/16	5/24/16
Modification –Consent forms modified to allow for tiered consent	6/7/16	6/24/16
Modification – addition of personnel (Raveena Vakil)	7/1/16	7/25/16
Modification – Approval for distribution of Patient Newsletter	9/9/16	9/20/16

NY State

The NYU PCBN maintains compliance with NY State Department of Health, which requires annual reports of activities, and reassurance on compliance with regulations. NYU PCBN renewed its official tissue bank license with the NY State Department of Health on August 19, 2016 (current expiration set for September 1, 2018).

HRPO

The NYU PCBN obtained its annual renewal through U.S. Army Medical Research and Materiel Command's (USAMRMC) Office of Research Protections (ORP), (Human Research Protection Office (HRPO) on 9/2/2016.

The rapid autopsy program at NYU Langone Medical center and Bellevue Hospital was renewed through the NYU IRB, while the program at the VA was renewed through the separate VA IRB. HRPO additionally maintains oversight of these programs related to the Use of Human Cadavers for Research Development Test & Evaluation (RDT&E). NY State Department of Health monitors the programs as well.

Regulatory Approval: Other collaborating sites

The NYU PCBN obtained IRB approval to add other sites as collaborating institutions (for access to archival material):

Woodhull Hospital: approved by NYU IRB on 9/23/2014
The Brooklyn Hospital: approved by TBH IRB on 2/23/2015
SUNY Downstate: approved by SUNY IRB on 06/15/2015 and by NYU IRB on 11/20/2015.
White Plains Hospital: The NYU PCBN applied for White Plains Hospital IRB approval and submitted an application and in addition, attended the board meeting (June 1st, 2016). After a lengthy delay, White Plains IRB rejected the application based on not meeting criteria in federal waiver 45 CFR 46.116. The NYU PCBN disagrees with this basis for denial and is in process to appeal the decision.

Contractual (Industrial Liaison) Approval: A material transfer agreement between NYU and SUNY Downstate was negotiated and approved (6/20/2016). This required requested changes to the website and assurances about commercial interactions.
Although IRB approval has been provided for Woodhull Hospital, The NYU PCBN awaits finance approval of the protocol. Initially proposed charges were unreasonably high so resolution of these charges was awaited to enable access without excessive consumption of grant funding. These discussions involved HHC (Hospitals and Health Authority of New York City) leadership and ultimately required a repeat application to HHC through its research portal. This remains under committee review, however is expected to be resolved within the coming month.

Outreach for access to archival material at other collaborating sites: The NYU site has arranged with the central HHC research leadership to assist in regulatory access to its various facilities. After discussion and meeting with the head of the research authority, Dr. Imah Jones, The NYU PCBN has been assured of its commitment to provide assistance in surmounting the regulatory/contractual hurdles that have delayed this process. The PI has recently been appointed as a committee member of the research council of HHC which should provide greater access and ability to expedite the process. .

B. **Accrual of Biospecimens (fresh frozen & formalin fixed paraffin embedded tissue and serum/plasma**

The NYU site accrues fresh and frozen tissue and biofluids including serum, plasma and urine at NYU Langone Medical Center, Bellevue and Manhattan and Brooklyn VA hospital.

The prospective accrual according to hospital site is detailed in table 2 below:

Table 2a: 2015- 2016 Accrual of Biospecimens by Hospital site	**NYU Total**	**BH Total**	**VA Total**	**Total**
Patients Consented	181	35	48	264
Surgery Performed	171	8	5	184
Frozen Tissue	155	8	5	168
Serum	123	20	155	298
Plasma	4	7	79	90
Buffy Coat	4	0	6	10
Urine	138	8	7	153
Prostatic Fluid	147	7	0	154
Seminal Vesicle Fluid	116	5	0	121

Table 2b: Accrual Biospecimens (NYU PCBN)	**2015**	**2016**	**Total Accrual since start of grant**
Patients Consented	218	264	482
Surgery Performed	175	184	359
Frozen Tissue	165	168	333
Serum	172	298	470
Plasma	15	90	105
Buffy Coat	15	10	25
Urine	92	153	245
Prostatic Fluid	119	154	273
Seminal Vesicle Fluid	86	121	207
Metastatic cases (RP LN) cases	11	12	23
ADT/chemo cases with longitudinal	28	31*	59
Rapid autopsy cases consented	9	5	14**

*16 are longitudinal and additional 15 others provided initial samples & are pending further visits

**3 subjects deceased (no NOK, 2 died out of state or no contact provided);1 withdrew consent (religious reasons); Therefore have a total of 10 alive participants consented to the rapid autopsy program

The accrual per quarter is shown in tables 3a – d below:

Table 3a: Biospecimen Acquisition Oct 1- Dec 31 2015	Total Specimens Collected
Serum	
Pre-Radical Prostatectomy	37
Metastatic	45
Total	**82**
Tissue	
Radical Prostatectomy	57
Fluids	
Prostatic fluid	47
Seminal Vesicle fluid	37
Urine (Pre-Radical Prostatectomy)	40
Total	**263**

Table 3b: Biospecimen Acquisition Jan 1 – March 31 2016	Total Specimens Collected
Serum	
Pre-Radical Prostatectomy	42
Metastatic	59
Total	**101**
Tissue	
Radical Prostatectomy	48
Fluids	
Prostatic fluid	42
Seminal Vesicle fluid	39
Urine (Pre-Radical Prostatectomy)	45
Total	**275**

Table 3c: Biospecimen Acquisition April 1– June 30 2016	Total Specimens Collected
Serum	
Pre-Radical Prostatectomy	41
Metastatic	26
Total	**67**
Tissue	
Radical Prostatectomy	37
Fluids	
Prostatic fluid	37
Seminal Vesicle fluid	28
Urine (Pre-Radical Prostatectomy)	37
Total	**206**

Table 3d: Biospecimen Acquisition July 1– Sept 30 2016	Total Specimens Collected
Serum	
Pre-Radical Prostatectomy	34
Metastatic	36
Total	**70**
Tissue	
Radical Prostatectomy	40
Fluids	
Prostatic fluid	34
Seminal Vesicle fluid	26
Urine (Pre-Radical Prostatectomy)	30
Total	**200**

The biospecimen procurement is a streamlined process at all three hospitals; with accrual volume reliant on several factors including clinical patient volume, treatment trends (specifically radical prostatectomy versus active surveillance) and subject recruitment. While the surgical specimen accrual is good and reaches expected metrics we continue to strive to enhance recruitment for different cohorts and facilities and reach out for greater efficiencies in the process. The higher accrual in 2016 over 2015 suggests these efforts have been rewarded (see Table 2b).

These efforts include implementation of a) systems for regular communication and alerts from Urology and Oncology of potential patients for recruitment (daily monitoring of patient schedules at three hospitals; frequent email communications with providers) b) tiered consents which allow patients to determine their individual choice as to level of participation c) consents translated into Chinese and Spanish in recognition of diverse patient backgrounds and home language. All these steps enable greater recruitment of potential subjects and foster trust that improves willingness for participation. The NYU PCBN also conducts educational seminars with

oncology and urology providers to promote awareness and encourage assistance with recruitment of subjects. An important influence on tissue accrual is of course of radical prostatectomy volume at each hospital. Even though there is a trend (nationwide) for decrease in radical prostatectomy volume, the NYU Langone Urology Department continues to attract more patient interest and has managed to increase its volume of surgical cases over the last year. In conjunction with this, The NYU PCBN is able to accrue a high percentage of potential cases. OF note,

The NYU PCBN has also begun to obtain consent and accrue active surveillance subjects as well as subjects treated by non-surgical means on clinical trials (HIFU treatment).

Over the past year, the NYU PCBN has taken steps to enhance patient interest in its rapid autopsy program. These include modifications of the consent form to allow the patient to provide permission for PCBN staff to contact their next of kin. In addition, the PCBN distributes an approved newsletter and links to its lab website to increase patient awareness. These steps enable further contact with next of kin and cultivate stronger relationships which are important to the rapid autopsy process.

C. **Specimen Characterization and Data annotation:**

In 2016, due to the limitations of the NYU PCBN database system, alternative relational database systems were investigated. The NYU PCBN initial positive experience with REDCAP suggested that it would satisfy many of the site's data needs and still be useful as a collaborative tool beyond NYU through open REDCAP.

Some advantages of REDCAP are: a) Allows secure and HIPAA compliant sharing of data by seamlessly removing identifiers b) Provides more security and quality assurance checks than current system offers c) Allows multiple individuals of our team to work on the database at the same time

As of June 2016, design of a NYU PCBN REDCAP database was completed. This consisted of implementation of data quality assurance steps, logic checks and algorithms and design of surveys that provide functionality to the database. The process of migration of data to REDCAP was started (9/1/16) and is underway with quality assurance steps to harmonize data.

NYU PCBN staff members regularly update clinical data through access to electronic medical records (EPIC, Quadramed and CPRS), Pathology databases (Powerpath & CoPath), Urology research databases and tumor registry records. Clinical data update is performed on a regular ongoing basis, with quality control checks (relook at a subset of cases) to assure accuracy. Additionally, tissue microarray data is updated on a regular basis (6 monthly for biochemical recurrence TMA).

NYU PCBN has begun to characterize prostate cancer using maps which allow 2 dimensional representation and characterization of focality (in preparation for multifocal TMA).

D. Specialized processing (Derivatives of biospecimens):

Tissue Microarrays (TMAs): The NYU site TMA sets that are part of PCBN continue to receive requests and are provided to investigators. Over the last year additional TMA sets have been completed at the NYU site while others are currently under construction (see Table 4).

Biochemical Recurrence (BCR) \TMA: The current TMA that NYU provides to PCBN investigators is a 217 case BCR TMA that enables assessment of biomarkers strongly associated with known prognostic factors (e.g. stage, grade). It includes patients with versus without biochemical recurrence, to a total of 217 cases, 23 with adjacent normal (4-5 tumor cores, 4 normal cores) and 13 BPH cases (4 cores). Since this TMA is frequently requested, NYU PCBN focused effort on construction of an expanded cohort BCR TMA. This is complete – providing a 645 case biochemical recurrence TMA (over 12 TMA Blocks, 4 cores for each case). The associated clinical data for this cohort has recently been aggregated and updated: 9% with biochemical recurrence, mean age = 59 years, 75% > 5year PSA follow-up, mean follow-up duration = 135 months.

Hormone Sensitivity TMA: The NYU site provides a 56 case Hormone sensitivity TMA, which enables testing of biomarkers associated with androgen biology. It includes hormone naive versus hormone refractory cases totaling 56 cases; 18 hormone resistant, 18 hormone naïve, 10 radical prostatectomy (RP) cases with neo adjuvant treatment, 10 RP without neo adjuvant treatment. Due to the rarity of castration resistant prostate cancer tissue samples, this TMA required searching across the entire archive of 3 major hospital sites for candidate cases. NYU PCBN continues to seek more partners with archival resources to enable identify more cases and is working to expand this TMA. Additional cases have been identified and the TMA awaits construction.

Multifocal TMA: The NYU site is working to construct a TMA that allows comparison of biomarkers across separately identifiable tumor foci. Prostate maps (with graphical representation of cancer distribution in the prostate) have been prepared through slide reconstruction to determine focality. Blocks have been retired and this TMA awaits construction.

HGPIN TMA: NYU PCBN has a current TMA however is preparing for expansion of this TMA cohort through an additional TMA. The challenges to this TMA are the requirement for pathologic characterization of tiny foci and identification of sufficiently large microscopic foci to allow accurate localization and sampling by a needle core into a TMA. The detailed work at identifying these tiny foci on slides and then matching to blocks is underway

Table 4: TMA preparation and construction over last year

Type of TMA	Design	Cohort size	Steps to tissue collection	Data extraction	Other derivatives	Challenges	Status
Expansion/ Addition of Hormone sensitivity TMA	Castration resistant tumor tissue from channel TURPs	Prior group = 18 resistant cases, additional 12 cases identified	Search through multiple databases and paper chart records, Archival off-site retrieval	Search of > 10 Electronic records and older paper charts	Storage of tissue cores for DNA & RNA extraction planned	Identification of cases	Awaiting additional case identification from partnering sites
HGPIN TMA	Foci of HGPIN in RP	60	Accurate pathologic characterization	Complete	None	Selection of minute foci and accurate	Selection & pathologic characterizat

	specimens					TMA Sampling	ion underway
Multifocal TMA	Select RP cases in 2015-16	30	Prostate cancer mapping (graphical representation of cancer foci)	Complete	Storage of tissue cores for DNA & RNA extraction planned		Awaiting construction
Grade/stage TMA	Consecutive RP cases 2015-16	100 cases	Current RP cases	Complete			Partially complete (1 block = 40 cases)
Biochemical Recurrence TMA	Consecutive RP cases 2005-2010	645		PSA follow-up		Clinical Follow-up	Completed

E. **Disbursement of Biospecimens (2015-16)**

Tissue microarray sets were provided to investigators as follows:

DATE	SPECIMEN	RECIPIENT
9/30/15	56 case Hormone Sensitivity TMA (3 sets)	Johns Hopkins University
11/23/15	56 case Hormone Sensitivity TMA (3 sets)	The Chinese University of Hong-Kong
12/8/15	Metastatic Frozen Tissue Samples (5 samples)	New York VA Medical Center
4/20/16	56 case Hormone Sensitivity TMA	University of Wisconsin
5/26/16	217 case Biochemical Recurrence TMA (2 sets)	New York University
6/20/16	217 case Biochemical Recurrence TMA (1 set)	New York University

Disbursement of biospecimens is primarily of tissue microarray sets. In order to make these more useful to investigators we have prepared product datasheets which outline the design, layout, construction, quality assurance steps and control tissues of the tissue microarrays. These datasheets are available for the biochemical recurrence and hormone sensitivity TMAs.

What opportunities for training and professional development has the project provided?

Several of the staff trained in database design and implementation skills for REDCAP and I2B2 implementation

How were the results disseminated to communities of interest?

Nothing to Report

What do you plan to do during the next reporting period to accomplish the goals?

If this is the final report, state "Nothing to Report."

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

We plan to 1) Continue accrual of biospecimens 2) To prepare tissue microarrays with associated data 3) To fully migrate NYU PCBN data to REDCAP 4) To increase rapid autopsy case recruitment and to 5) To bring on more partnering sites for access to archival prostate cancer tissue 6) Expand the resource to include active surveillance patients as well as patients on clinical trials such as focal therapy trial (HIFU).

F. **IMPACT:** Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:

What was the impact on the development of the principal discipline(s) of the project?

Nothing to Report

What was the impact on other disciplines?

Nothing to Report

What was the impact on technology transfer?

.

Nothing to Report

What was the impact on society beyond science and technology?

.

Nothing to Report

G. **CHANGES/PROBLEMS:** The Project Director/Principal Investigator (PD/PI) is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:

Changes in approach and reasons for change
Describe any changes in approach during the reporting period and reasons for these changes. Remember that significant changes in objectives and scope require prior approval of the agency.

Due to the low activity in the rapid autopsy program, our group has sought more opportunities to recruit patients with metastatic prostate cancer and approval for more frequent contact and communication with next of kin to maintain interest and cooperation in this program. We have sought to advance our data capture methods and data system (migration to REDCAP) in concert with expansion of institutional bioinformatics resources.

Actual or anticipated problems or delays and actions or plans to resolve them
Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

Due to space constraints at our institution, storage of paraffin blocks and slides > 1-year prior is at an offsite commercial facility in New Jersey. The retrieval charges ($35 per case) become onerous when a large number of cases is requested, which is often the case in preparation for TMA construction. We therefore are reorganizing our approach to collection of paraffin material to avoid need for repeated retrieval.

Changes that had a significant impact on expenditures
Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

Nothing to report

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Significant changes in use or care of human subjects

Nothing to Report

Significant changes in use or care of vertebrate animals.

Not applicable

Significant changes in use of biohazards and/or select agents

None reported

H. **PRODUCTS:** List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."

- **Publications, conference papers, and presentations**

Journal publications

Fang-Ming Deng, Nicholas M. Donin, Ruth Pe Benito, Jonathan Melamed, Julien Le Nobin, Ming Zhou, Sisi Ma, Jinhua Wang, Herbert Lepor, Size-adjusted Quantitative Gleason Score as a Predictor of Biochemical Recurrence after Radical Prostatectomy, **European Urology**, Volume 70, Issue 2, August 2016, Pages 248-253

Sridharan S, Macias V, Tangella K, et al. Prediction of prostate cancer recurrence using quantitative phase imaging: Validation on a general population. ***Scientific Reports***. 2016;6:33818.

Books or other non-periodical, one-time publications.

Nothing to Report

Other publications, conference papers, and presentations.

Nothing to Report

- **Website(s) or other Internet site(s)**

Nothing to Report

- **Technologies or techniques**

Nothing to Report

- **Inventions, patent applications, and/or licenses**

Nothing to Report

- **Other Product**

Research material: Biospecimen accrual – see table	
Type of biospecimen	Number
Frozen Tissue	168
Serum	298
Plasma	90
Buffy Coat	10
Urine	153
Prostatic Fluid	154

I. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change."

Name: *Jonathan Melamed MD*
Project Role: *PI*
Researcher Identifier (ORCID ID): orcid.org/0000-0003-2844-7990
Nearest person month worked: *3*
Contribution to Project: *Dr. Melamed has oversight of project*

Name: *Peng Lee MD PhD*
Project Role: *Co-investigator*
Researcher Identifier (e.g. ORCID ID): 1234567
Nearest person month worked: *3*
Contribution to Project: *Dr. Lee oversees activities at the NY Harbor VA.*

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Name: *Emily Dube, BS*
Project Role: *Biorepository* manager
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *10*
Contribution to Project: *Ms. Dube* manages and oversees the day-to-day functioning of the Cancer Biorepository and *is* responsible for biofluid and tissue procurement, data extraction for the existing paraffin embedded cases in NYU archives and data entry of new cases into IRB compliant database.

Name: *Raveena Vakil, BS*
Project Role: *Research coordinator*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *3*
Contribution to Project: *Ms. Vakil is* responsible for biofluid and tissue procurement, data extraction for the existing paraffin embedded cases in NYU archives and data entry of new cases into IRB compliant database.

Name: *Diane Wisniewski, HT (ASCP)*
Project Role: *Research Technician*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *10*
Contribution to Project: *Ms. Wisniewski is responsible for histology, tissue microarray construction, cryotomy, microtomy & immunohistochemistry staining.*

Name: *Lena Kleyn, BS*
Project Role: *Research coordinator*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *7*
Contribution to Project: *Ms. Kleyn was* responsible for biofluid and tissue procurement (in role now currently filled by Ms. Vakil).

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Nothing to report

What other organizations were involved as partners?

Organization Name: The Brooklyn Hospital
Location of Organization: Brooklyn, New York
Partner's contribution to the project: Collaboration

Organization Name: SUNY Downstate Hospital
Location of Organization: Brooklyn, New York
Partner's contribution to the project: Collaboration

Organization Name: Brooklyn VA Hospital
Location of Organization: Brooklyn, New York
Partner's contribution to the project: Collaboration

J. **SPECIAL REPORTING REQUIREMENTS**

COLLABORATIVE AWARDS: For collaborative awards, independent reports are required from BOTH the Initiating PI and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to **https://ers.amedd.army.mil** for each unique award.

QUAD CHARTS: If applicable, the Quad Chart (available on https://www.usamraa.army.mil) should be updated and submitted with attachments.

K. **APPENDICES:** Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.

EUROPEAN UROLOGY 70 (2016) 248–253

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Platinum Priority – Prostate Cancer

Editorial by Bruno Nahar, Nachiketh Prakash Soodana and Sanoj Punnen on pp. 254–255 of this issue

Size-adjusted Quantitative Gleason Score as a Predictor of Biochemical Recurrence after Radical Prostatectomy

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Abstract

Background: The risk of biochemical recurrence (BCR) following radical prostatectomy for pathologic Gleason 7 prostate cancer varies according to the proportion of Gleason 4 component.
Objective: We sought to explore the value of several novel quantitative metrics of Gleason 4 disease for the prediction of BCR in men with Gleason 7 disease.
Design, setting, and participants: We analyzed a cohort of 2630 radical prostatectomy cases from 1990–2007. All pathologic Gleason 7 cases were identified and assessed for quantity of Gleason pattern 4. Three methods were used to quantify the extent of Gleason 4: a quantitative Gleason score (qGS) based on the proportion of tumor composed of Gleason pattern 4, a size-weighted score (swGS) incorporating the overall quantity of Gleason 4, and a size index (siGS) incorporating the quantity of Gleason 4 based on the index lesion.
Outcome measurements and statistical analysis: Associations between the above metrics and BCR were evaluated using Cox proportional hazards regression analysis.
Results and limitations: qGS, swGS, and siGS were significantly associated with BCR on multivariate analysis when adjusted for traditional Gleason score, age, prostate specific antigen, surgical margin, and stage. Using Harrell's c-index to compare the scoring systems, qGS (0.83), swGS (0.84), and siGS (0.84) all performed better than the traditional Gleason score (0.82).
Conclusions: Quantitative measures of Gleason pattern 4 predict BCR better than the traditional Gleason score.
Patient summary: In men with Gleason 7 prostate cancer, quantitative analysis of the proportion of Gleason pattern 4 (quantitative Gleason score), as well as size-weighted measurement of Gleason 4 (size-weighted Gleason score), and a size-weighted measurement of Gleason 4 based on the largest tumor nodule significantly improve the predicted risk of biochemical recurrence compared with the traditional Gleason score.

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Prediction of prostate cancer recurrence using quantitative phase imaging: Validation on a general population

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Prediction of biochemical recurrence risk of prostate cancer following radical prostatectomy is critical for determining whether the patient would benefit from adjuvant treatments. Various nomograms exist today for identifying individuals at higher risk for recurrence; however, an optimistic underestimation of recurrence risk is a common problem associated with these methods. We previously showed that anisotropy of light scattering measured using quantitative phase imaging, in the stromal layer adjacent to cancerous glands, is predictive of recurrence. That nested-case controlled study consisted of specimens specifically chosen such that the current prognostic methods fail. Here we report on validating the utility of optical anisotropy for prediction of prostate cancer recurrence in a general population of 192 patients, with 17% probability of recurrence. Our results show that our method can identify recurrent cases with 73% sensitivity and 72% specificity, which is comparable to that of CAPRA-S, a current state of the art method, in the same population. However, our results show that optical anisotropy outperforms CAPRA-S for patients with Gleason grades 7–10. In essence, we demonstrate that anisotropy is a better biomarker for identifying high-risk cases, while Gleason grade is better suited for selecting non-recurrence. Therefore, we propose that anisotropy and current techniques be used together to maximize prediction accuracy.

In 2010, 138,000 men in the USA underwent radical prostatectomy for treatment of prostate cancer[1]. Biochemical recurrence or increase in serum prostate specific antigen (PSA) levels after prostatectomy is an early sign of prostate cancer recurrence. 17–33% of patients who undergo radical prostatectomy as primary form of treatment experience a biochemical recurrence of prostate cancer and 29–34% of individuals in that cohort will have metastatic prostate cancer with bone as the most common site of metastasis[2–6]. The 5-year survival rate for metastatic prostate cancer is 25–43%[3,7]. Identification of individuals at high risk for biochemical recurrence will enable early adjuvant treatment for those patients, and thus reduce the risk for metastatic disease and prostate cancer-specific mortality.

Various methods based on pre and post-surgical evaluation of prostate tissue and clinical parameters have been developed for prediction of biochemical recurrence and these techniques have been reviewed elsewhere[8,9]. The post-prostatectomy biochemical recurrence prediction methods which are most widely reported and validated are the Stephenson nomogram and CAPRA-S which have concordance index values reported between 0.72–0.77[9,10]. Optimistic prediction of non-recurrence is a problem that has previously been noted in both methods, despite the high discrimination accuracy[9,11]. Additionally, these methods can lead to erroneous results as

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